REMARKS

Claims 13-16, 26, and 27 are currently pending. With this Amendment, claims 14 and 26 have been cancelled without prejudice. Applicants reserve the right to pursue the subject matter of the cancelled claims in one or more related applications. New claim 28 has been added. Support for new claim 28 can be found throughout the specification as filed and, in particular, at page 3, *ll.* 11-22; page 8, *ll.* 18-28; and Example 1. Claim 13 has been amended to incorporate the phrase "endogenously expressed" as it relates to estrogen-regulated markers and to indicate that the estrogen-regulated markers used in accordance with the invention are selected from the group consisting of SEQ ID NOs:1-75. Support for the amendments to claim 13 can be found throughout the specification as filed and, in particular, at page 18, *ll.* 27-30; page 4, *ll.* 11-26; page 5, *ll.* 3-9; and page 11, *ll.* 23-28. Applicants assert that no new matter has been introduced by these claim amendments. Upon entry of this Amendment, claims 13, 15, 16, 27, and 28 will be pending.

Applicants request consideration and entry of the amendments and remarks into the record.

I. INTERVIEW SUMMARY

Applicants thank Examiner Pak for the telephone interview of January 24, 2008. As indicated in the Examiner's Interview Summary mailed February 6, 2008, Applicants stated during the interview that Mendelsohn, et al. (U.S. Patent No. 5,728,534; "Mendelsohn") does not teach the claimed invention. Applicants herein add that during the interview, Applicants clarified to the Examiner that the present invention is *not* directed toward the discovery of the nucleic acid sequences of estrogen-regulated markers ("ERMs"), *i.e.*, those disclosed, for example, in Table I. Rather, the claimed invention is based on Applicants' discovery that certain *known* nucleic acid sequences encode ERMs and, as a consequence, these nucleic acid sequences

and the proteins that they encode can be utilized in methods for identifying and/or screening compounds having estrogenic and/or anti-estrogenic activity, *i.e.*, SERMs. As pointed out by Applicants, the functions of the proteins encoded by these nucleic acids are *not* relevant to the claimed invention. What is relevant is that each ERM identified in Table I (as SEQ ID NOs:1-75) was found to be responsive to estrogen treatment using the assays described in the specification. See Example II and Table I of the specification as originally filed. Thus, the expression level of said ERMs can be measured in accordance with the methods of the invention as a means to screen for candidate SERMs.

II. THE REJECTION FOR LACK OF WRITTEN DESCRIPTION SHOULD BE WITHDRAWN

Claims 13, 15-16, and 26-27 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to provide a sufficient written description. In particular, the Examiner contends that the specification lacks written description for "nucleic acid sequences which have not been identified by function (*i.e.* orphan proteins) such as SEQ ID NO:1 [which] can be used as regulated sequence of the estrogen modulation but the function of SEQ ID NO:1 is not known," which the Examiner alleges is the essential feature of the claimed invention. For at least the reasons set forth below, Applicants respectfully disagree with the Examiner.

A. The Legal Standard

The test for sufficiency of written description is whether the disclosure of the application "reasonably conveys to the artisan that the inventor had possession" of the claimed subject matter. *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983); accord *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563; see also, *Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985). The Court of Appeals for the Federal Circuit has repeatedly considered the written description requirement and consistently found that exacting detail is not

necessary to meet the requirement. *See, e.g., In re Alton*, 76 F.3d 1168, 1175 (Fed. Cir. 1996) (stating that "[i]f a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, *even if [not] every nuance of the claims is explicitly described in the specification*, the adequate written description requirement is met") (emphasis added).

Furthermore, in accordance with the Guidelines for Examination of Patent Applications Under 35 U.S.C. 112 ¶ 1, "Written Description Requirement," what is *conventional or well known to one of skill in the art* need not be disclosed in detail (*Id.* at p. 1105, column 3, *ll.* 39-41, emphasis added) and, where the *level of knowledge and skill in the art is high*, a written description question should not be raised. *Id.* at p. 1106, column 1, *ll.* 34-36. *See also Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005) (emphasis added).

B. The Claims Comply with the Written Description Requirement

At the outset, Applicants respectfully point out that the Examiner has seemingly misapplied the legal standard for written description under 35 U.S.C. § 112, first paragraph, and that the Examiner's rejection as written is, in fact, an enablement rejection.

Moreover, Applicants assert that the specification as filed sufficiently satisfies the written description requirement. As discussed in the Interview Summary above, the claimed invention is based on Applicants' discovery that certain *known* nucleic acid sequences encode ERMs and, as a consequence, these nucleic acid sequences and the proteins that they encode can be utilized in methods for identifying and/or screening compounds having estrogenic and/or anti-estrogenic activity, *i.e.*, SERMs. As indicated, the functions of the proteins encoded by these nucleic acids are not relevant to claimed invention. What is relevant is that each ERM identified in Table I (as SEQ ID NOs:1-75) was found to be responsive to estrogen treatment using the assays described in the specification. See Example II and Table I of the specification as

originally filed. Thus, the expression level of said ERMs can be measured in accordance with the methods of the invention as a means to screen for candidate SERMs.

The specification provides several art-accepted methods for determining a change in the expression level of an ERM gene and/or its corresponding protein in a cell in response to a SERM, *e.g.*, an RNAse protection assay, Western Blot analysis, PCR, a reporter gene assay, and ELISA. The specification further provides a working example (Example 4) demonstrating how a candidate SERM can be tested for having estrogenic activity in accordance with the screening methods of the claimed invention. Given that the specification provides the nucleic acid sequences of the ERMs to be utilized in accordance with the methods of the invention, *i.e.*, SEQ ID NOs:1-75; provides methods by which ERM gene and/or protein expression can be measured; and gives a working example demonstrating that the screening methods of the instant invention can be used to identify candidate SERMs, Applicants assert that it would be clear to one of skill in the art that the inventors did, indeed, have possession of the claimed invention at the time of filing.

For at least the foregoing reasons, Applicants submit that the instant pending claims sufficiently satisfy the written description requirement and respectfully request that the rejection of these claims under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, be withdrawn.

III. THE REJECTION FOR LACK OF ENABLEMENT SHOULD BE WITHDRAWN

Claims 13-16 and 26-27 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, the Examiner contends that the invention is not enabled because the claims are allegedly drawn generically to any ERM and not specific species

and because the functions of the specific species of ERMs are not known. For at least the reasons set forth below, Applicants respectfully disagree with the Examiner.

A. The Legal Standard

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988). In fact, well known subject matter is preferably omitted. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well known in the art."). Further, one skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. *See Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990) ("A decision on the issue of enablement requires determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent Applicant to "set forth every minute detail regarding the invention." *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278, 1291 (D. Del. 1991); *see also DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985).

Undue experimentation is experimentation that would require a level of ingenuity *beyond* what is expected from one of ordinary skill in the field. *Fields v. Conover,* 170 USPQ 276, 279 (CCPA 1971). As referenced by the Examiner, the factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands,* 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of

pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

Further, while the predictability of the *art* can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the *result* of an experiment is *not* a consideration. Indeed, the Court of Custom and Patent Appeals in *In re Angstadt,* has specifically cautioned that the unpredictability of the result of an experiment is *not* a basis to conclude that the amount of experimentation is undue. In particular, in an unpredictable art it is not necessary for an inventor to disclose a test with every *species* covered by a claim, as it would force an inventor seeking adequate patent protection to carry out a prohibitive number of experiments – and discourage inventors from filing applications in an unpredictable area. *In re Angstadt,* 190 USPQ 214 (CCPA 1976).

B. The Claimed Invention Is Fully Enabled

Although Applicants do not acquiesce to the propriety of the Examiner's rejection, in order to expedite prosecution, the claims have been amended and are now drawn to a method wherein the level of expression of an ERM selected from the group consisting of SEQ ID NOs:1-75 is determined (see claim 13 as amended and claims dependent therefrom). These 75 ERMs were identified by assays disclosed in the specification to be responsive to estrogen treatment (see Example 2 and Table I of the originally filed specification). Applicants assert that this amendment serves to overcome the Examiner's rejection of the claims for allegedly being drawn generically to any ERM and not specific species.

Furthermore, Applicants assert that in their rejection of the claims for being drawn to ERMs that allegedly have no known function, the Examiner has mischaracterized the invention. As discussed in the Interview Summary and in the response to the Examiner's

rejection of the claims for lack of adequate written description, the claimed invention is based on methods for identifying and/or screening compounds having estrogenic and/or anti-estrogenic activity, *i.e.*, SERMs, wherein estrogenic activity can be determined by measuring the nucleic acid and/or protein expression level of ERMs. Applicants again point out to the Examiner that the function of these ERMs is *irrelevant* and that to practice the claimed invention, a person skilled in the art would need only to employ methods that allow ERM nucleic acid and/or protein expression to be measured. As discussed above, such methods are well-known in the art. Furthermore, the specification is replete with methods to detect differential gene expression, both at the nucleic acid *and* protein level, in response to treatment with estrogen and/or a SERM. Methods for measuring nucleic acids (*e.g.*, mRNA, cDNA or DNA) of estrogen-responsive genes include, but are not limited to, the use of gene chips (*e.g.*, the UniGEM technology; *see* pp. 11-12; and Example 2 of the originally filed specification); reporter gene assays where a gene encoding an ERM or ERM-related protein is isolated and linked to various operably linked reporter genes (*e.g.*, luciferase, CAT; *see* pp. 14-15); RNase protection assays (*see* p. 18); and PCR (*see* p. 26). The specification further provides a working example (Example 4) that discloses the use of ERMs identified by the methods of the invention for identifying agents with estrogenic activity using an RNase protection assay (pp. 70-72).

For at least the foregoing reasons, Applicants submit that the instant pending claims are fully enabled and respectfully request that the rejection of these claims under 35 U.S.C. § 112, first paragraph, for lack of enablement, be withdrawn.

IV. THE REJECTION FOR ANTICIPATION SHOULD BE WITHDRAWN

The Examiner has rejected claims 13, 15-17, and 26 under 35 U.S.C. 102(b) as being anticipated by Mendelsohn. For at least the reasons set forth below, Applicants respectfully disagree with the Examiner.

A. The Legal Standard

An anticipating reference must describe and enable the claimed invention, including all the claim limitations, with sufficient clarity and detail to establish that the subject matter already existed in the prior art and that its existence was recognized by persons of skill in the art. *In re Spada*, 911 F.2d 705, 708, 15 U.S.P.Q.2d 1655, 1657 (Fed. Cir. 1990); *Crown Operations International, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1375, 62 U.S.P.Q.2d 1917, 1921 (Fed. Cir. 2002). The standard for an anticipatory reference is set forth in *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987): "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See also Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989) (holding that "[t]he identical invention must be shown in as complete detail as is contained in the...claim"). Further, the anticipating reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter. *PPG Industries, Inc. v. Guardian Industries Corp.* 75 F.3d 1558, 1564, 37 U.S.P.Q.2d 1618, 1623 (Fed. Cir. 1996).

B. Mendelsohn Does Not Teach the Claimed Invention

As previously pointed out to the Examiner, the assays described in Mendelsohn require a non-native reporter construct containing an upstream regulatory region of an estrogen receptor responsive gene, or an isolated estrogen receptor recognition element operably linked to a nucleotide sequence encoding a detectable protein (*see, e.g.*, column 8, *ll.* 62-64; column 9, *ll.* 32-34). In contrast, the assays of the claimed invention teach determination of the expression levels of an *endogenously*-expressed ERM in response to treatment with a candidate SERM or estrogen. The Examiner contends that because the claims are not limited to endogenously-expressed ERMs, they are anticipated by Mendelsohn. Although Applicants do not acquiesce to

the propriety of this rejection, in order to expedite prosecution, the claims have been amended to include the limitation that the ERM is endogenously-expressed (see claim 13 as amended and claims dependent therefrom).

For at least the foregoing reasons, Applicants submit that the instant pending claims are not anticipated by Mendelsohn and request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

CONCLUSION

Applicant respectfully requests entry and consideration of the foregoing amendments and remarks. No new matter has been introduced. The claims are believed to be free of the art and patentable. Withdrawal of all the rejections and an allowance are earnestly sought. Should any questions remain, the Examiner is invited to telephone the undersigned at the number indicated below.

Respectfully submitted,

Date: April 30, 2008

Anthony M. Insogna 35,203
Anthony M. Insogna (Reg. No.)

By: Lynda Nguyen 54,338
Lynda Q. Nguyen (Reg. No.)

JONES DAY
222 East 41st Street
New York, New York 10017
(212) 326-3939

Enclosures